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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,535	08/26/2005	Lorne J Brandes	3172-103	5333

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
02/26/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/526,535	BRANDES, LORNE J	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed **12/3/07**presents remarks and arguments to the office action mailed **6/1/07**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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Status of Claims

Claims 1-19 are pending and are examined in this office action.

Specification

The amendment to the specification has been received and acknowledged with regard to the trademark.

Maintained *Claim Rejections - 35 USC § 103*

Applicant argues that: "The Brandes reference teaches a chemotherapeutic treatment of cancer cells - inflammatory breast cancer (cell tumors are inflammatory (see col. 12, line 53 and col. 11, lines 60 to 61)." The applicant

points out that while col. 11, lines 60 to 61, describe the treatment of breast cancer, col. 12, line 53 summarizes the results of Example X, which illustrates the tumor promoting and pro-inflammatory response effects of DPPE (a diphenyl compound falling within the scope of the formula in claim 1) alone. There is no cancer treatment in this Example, that the result clearly shows that DPPE enhances inflammatory response of tumor promoter PMA.

Also that the Brandes reference does not teach the specific combination, nor does the abstract teach neoduvant treatment.

With regard to the Vincent reference, Applicant argues that the abstract as relied upon teaches the use of DPPE in neoadjuvant treatment refers to a post surgical treatment and not a neoadjuvant therapy.

That Koo et al. is silent as to the possibility of a combination of anthracylines and taxanes and as to the neoadjuvant treatment of specific forms of breast cancer.

That the Beer et al. is concerned with prostrate cancer and that the claims are directed to breast cancer a female condition.

In summary that the combined art dot not suggest the present invention.

In response, with regard to the Brandes reference, the abstract teaches the invio treatment of cancer cells with a DPPE in combination with a chemotherapeutic agent specifically illustrated. Without adhering to the term neoadjuvant, the combination of DPPE and daunorubicin/adriamycin are used both of which are anthracyclines. See col. 9, lines 40-45. Treatment of breast cancer is taught, see col. 11, lines 42-45, one of ordinary skill in the art would be motivated to administer DPPE to inhibit binding of

intracellular histamine and subsequent administration of at least one chemotherapeutic agent in an amount toxic for the cancer.

Examiner, then combines Vincent which teaches DPPE is administered prior to administering chemotherapeutic agents intravenously about 30-90 minutes prior to administration (see para. 0100). Para. 0039-0041 teaches graphical representation of DPPE with doxorubicin another type of anthracycline chemotherapeutic agent. Further, see para 0079, the reference teaches DPPE in conjuction with one or more chemotherapeutic agents as a part of neodjuvant therapy.

Khoo et al. is used to show that the compounds have been used in a chemotherapeutic treatment that required administration at intervals of about 21-28 days as required by instant claim 19.

While it is true that the Beer et al. teaching is related to prostate cancer a male disease, non the less the teaching also recite that adjuvant therapy showed greater impact. See page 189 rt. col. last para., line4-the end. The reference was used to show mainly that the compounds have been used before in a neoadjuvant therapy.

This is a 103 rejection, it is the combination of what is known in the art. All the recited art teach the use of DPPE with anthracycline , wherein the cancer is breast and is given at intervals.

Careful consideration has been given to the argument, however, found not persuasive. The rejection is maintained and repeated as in the office action of record.

Claims **1-19** remain rejected under 35 U.S.C. 103(a) as being unpatentable over Brandes US 5,618,846 taken with Vincent 2004/0248986 and Khoo et al. *Journal of*

Clinical Oncology, Vol 17, Issue 11 (November), 1999: 3431-3437(submitted IDS) in view of Beer et al. The prostrate 45: 184-193 (2000).

With regards to the instant claim 1 the Brandes reference teaches a chemotherapeutic treatment of cancer cells- inflammatory breast cancer (all tumors are inflammatory (see col. 12, lines 53 and col. 11, line 60-61) comprising administering the a diphenyl compound (DPPE)  (see col. 3, lines 10-15) as in the instant claim 1, wherein X and Y are each chlorine, Z is an alkylene, from 103 carbon atoms or C=O and R1 and R2 are each alkyl (see col. 3, lines 17-22) followed by a sufficient time (see col. 4 lines 10-13) subsequently administering an anthracycline chemotherapeutic agent (see col. 4, lines 10-13). With regards to claims 2 and 3, the reference teaches  (see col. 3, lines 45-50) having the same substituents as that of the instant claimed invention, wherein the diphenyl is a hydrochloride salt (see col. 3, lines 53-55) as in claim 4. As to the instant claims 5-6 the antracycline chemotherapeutic agent is daunorubicin (see col. 9, Table IV). One of ordinary skill in the art would have been motivated to switch daunorubicin with that of doxorubicin because both are chemotherapeutic drugs from the same family anthracycline, both are used in cancer treatment and would have expected a successful result in doing so. Nothing unobvious is seen in switching one drug that has the same

property in the same family with another of the same family. The reference also used adriamycin-which is doxorubicin (see col. 7, lines 40-45).

The Brandes reference further teaches the compound (N, N-diethyl-2-[4-(phenylmethyl)-phenoxy]ethanamine monohydrchloride (DPPE) is administered 30-90 minutes prior to the chemotherapeutic agent (see col. 4, lines 40-42) as in the instant claims 8 and 9-11 and the DPPE is administered intravenously (see col. 5, line 20). The Brandes reference also teaches with regards to claim 8 DPPE is administered prior to administering chemotherapeutic agent DPPE is administered about 8 to 240 mg/M^2 (see col. 4, lines 50-53) wherein the amount is 1-6 mg/kg (see col. 11, lines 10-12) which is within the claim limitation of 3-10 mg/kg as in claims 14 and 15-16. Adriamycin is the registered name for doxorubicin is administered 60 mg/ mg/M^2 (see col. 11, lines 19-20) as in claim 17 in part and 8 and 240 mg/M^2 (see col. 4, lines 50-54) as in the instant claim 13. The reference did not teach the use of a second chemotherapeutic agent, however suggested that the invention is widely applicable to any type of chemotherapeutic drug (see col. 4, lines 25-27). The above reference lacks the teaching of administering the chemotherapeutic treatment in a number of cycles

The term neoadjuvant is meant a treatment that is given first to help make the next treatment step go more smoothly, this type of therapy is mainly used to shrink a large tumor before radiation or surgery as taught by the reference (see abstract) wherein the treatment is carried out to inhibit normal cell proliferation.

Vincent teaches the use of DPPE (see abstract) in a neoadjuvant treatment (see abstract).

DPPE as referred to is the drug compound/formula in claims 1-4. Vincent reference teaches DPPE is administered prior to administering chemotherapeutic agents intravenously about 30-90 minutes prior to administration (see para. 0100) as in claims 8-11, wherein the anthracycline agent is doxorubicin or epirubicin (see para 0084) and taxane (see 0084) wherein the taxane is paclitaxel or docetaxel (see 0082) as taxol or taxotere as in claims 5-7, thus claim 10 is obvious. The reference further teaches that doxorubicin is administered 60-90 mg as in instant claim 17 (see para 0104) about 20 minutes as in claim 12, wherein the regimen is once for 3 weeks-thus 21 days and number of cycle is from 2-10 which is within the claim limitation of 19 (see para 0104). The reference, however did not teach the taxane is taxol or taxotere, however, the drug family is well known in the art of cancer so using taxane will result in the use of either taxol or taxotere such as paclitaxel or docetaxel (see NCI taxanes in cancer treatment).

Khoo et al. teach administering a DPPE followed by the administration of doxorubicin every 21 days for a maximum of seven cycles which is within the claim limitation of the instant claim 19 (see page 3431 higlighted sec).

One of ordinary skill in the art would be motivated to combine the Khoo et al reference with Vincent and administer the chemotherapy agents in a cycle because administering such agents in a treatment regimen is taught by Khoo et al. Therefore one of ordinary skill in the art would be motivated to do so and expect success because it has been taught by Khoo et al.

Beer et al. teach neodjuvant therapy (see page 186 highlighted sec) in patients undergoing prostectomy, and also the patient population with breast cancer (see page 189, rt. col. highlighted sec), wherein the combination chemotherapy includes the use of DPPE with taxanes such as paclitaxel and docetaxel. Beer et al also teach administering a taxane taught as (docetaxel or paclitaxel) in the range 75 mg/m^2 (see highlighted sec-pg 187) as in claims 17 and 18. The references use taxol which is paclitaxel as claimed, one of ordinary skill in the art would be motivated to substitute the taxane for taxol or taxotere because taxane, taxol and taxotere belong to a group of chemotherapy drugs and are well known in the art of oncology (see supporting doc. NCI enclosed).

Brandes, lack the teaching of specifically incorporating a taxane, but teaches that any chemotherapeutic agent can be use, thus one of ordinary skill in the art would be motivated to combine the Beer et al., dosage for a docetaxel/paclitaxel. One of ordinary skill in the art would be motivated to use a chemotherapeutic agent use a taxols administer the treatment dosages as taught by both references and expect a successful result because both references teaches the ranges of the drugs and combination is taught by Brandes.

One of ordinary skill in the art would have been motivated to combine the above cited prior art and use a taxol (paclitaxel) as taught by Beer because as taught by Brandes the invention is widely applicable to any type of chemotherapeutic drug (see col. 4, lines 25-27) therefore nothing unobvious is seen in the combination.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made for neoadjuvant chemotherapy in patients with inflammatory breast cancer.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
2/6/08

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614